JC10 Rec'd PCT/PTO 02 JAN 2002

FORM PTO-1390 (REV. 9-2001) U S DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE

# TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371

| | | |
|---|---|---|
| ATTORNEY'S DOCKET NUMBER Mo-6888/LeA 33,693 | | |
| U.S. APPLICATION NO. (If known, see 37 CFR 1.5 To Be Assigned 10/030365 | | |
| INTERNATIONAL APPLICATION NO. PCT/EP00/05829 | INTERNATIONAL FILING DATE 23 June 2000 (23.06.00) | PRIORITY DATE CLAIMED 05 July 1999 (5.07.99) |

TITLE OF INVENTION
METHOD FOR OXIDATING ORGANIC COMPOUNDS

APPLICANT(S) FOR DO/EO/US LANGER, Reinhard; KLAUSENER, Alexander and RODEFELD, Lars

Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. [X] This is a **FIRST** submission of items concerning a filing under 35 U.S.C. 371.
2. [ ] This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing under 35 U.S.C. 371.
3. [X] This is an express request to begin national examination procedures (35 U.S.C. 371(f)). The submission must include items (5), (6), (9) and (21) indicated below.
4. [X] The US has been elected by the expiration of 19 months from the priority date (Article 31).
5. [X] A copy of the International Application as filed (35 U.S.C. 371(c)(2))
   a. [X] is attached hereto (required only if not communicated by the International Bureau).
   b. [ ] has been communicated by the International Bureau.
   c. [ ] is not required, as the application was filed in the United States Receiving Office (RO/US).
6. [X] An English language translation of the International Application as filed (35 U.S.C. 371(c)(2)).
   a. [X] is attached hereto.
   b. [ ] has been previously submitted under 35 U.S.C. 154(d)(4).
7. [ ] Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3))
   a. [ ] are attached hereto (required only if not communicated by the International Bureau).
   b. [ ] have been communicated by the International Bureau.
   c. [ ] have not been made; however, the time limit for making such amendments has NOT expired.
   d. [ ] have not been made and will not be made.
8. [ ] An English language translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371 (c)(3)).
9. [X] An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)).
10. [ ] An English language translation of the annexes of the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).

**Items 11 to 20 below concern document(s) or information included:**

11. [ ] An Information Disclosure Statement under 37 CFR 1.97 and 1.98.
12. [X] An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.
13. [X] A FIRST preliminary amendment.
14. [ ] A SECOND or SUBSEQUENT preliminary amendment.
15. [ ] A substitute specification.
16. [ ] A change of power of attorney and/or address letter.
17. [ ] A computer-readable form of the sequence listing in accordance with PCT Rule 13ter.2 and 35 U.S.C. 1.821 - 1.825.
18. [ ] A second copy of the published international application under 35 U.S.C. 154(d)(4).
19. [ ] A second copy of the English language translation of the international application under 35 U.S.C. 154(d)(4).
20. [ ] Other items or information:

| U S APPLICATION NO (if known, see 37 CFR 1.5) | INTERNATIONAL APPLICATION NO. | ATTORNEY'S DOCKET NUMBER |
|---|---|---|
| To Be Assigned 10/030365 | PCT/EP00/05829 | Mo-6888/LeA 33,693 |

JC10 Rec'd PCT/PTO 02 JAN 2002

21. [X] The following fees are submitted:

**BASIC NATIONAL FEE (37 CFR 1.492 (a) (1) - (5)):**

| | | CALCULATIONS | PTO USE ONLY |
|---|---|---|---|
| Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO and International Search Report not prepared by the EPO or JPO . . . . . . . . . . | **$1040.00** | | |
| International preliminary examination fee (37 CFR 1.482) not paid to USPTO but International Search Report prepared by the EPO or JPO . . . . . . . . | **$890.00** | | |
| International preliminary examination fee (37 CFR 1.482) not paid to USPTO but international search fee (37 CFR 1.445(a)(2)) paid to USPTO . . . . . . . . . . | **$740.00** | | |
| International preliminary examination fee (37 CFR 1.482) paid to USPTO but all claims did not satisfy provisions of PCT Article 33(1)-(4) . . . . . . . . . | **$710.00** | | |
| International preliminary examination fee (37 CFR 1.482) paid to USPTO and all claims satisfied provisions of PCT Article 33(1)-(4) . . . . . . . . . . . . . . . | **$100.00** | | |
| **ENTER APPROPRIATE BASIC FEE AMOUNT =** | | $ 890.00 | |
| Surcharge of **$130.00** for furnishing the oath or declaration later than [ ] 20 [ ] 30 months from the earliest claimed priority date (37 CFR 1.492(e)). | | $ 0.00 | |

| CLAIMS | NUMBER FILED | NUMBER EXTRA | RATE | | |
|---|---|---|---|---|---|
| | | | | $ | |
| Total claims | 13 - 20 = | 0 | x **$18.00** | $ 0.00 | |
| Independent claims | 1 - 3 = | 0 | x **$84.00** | $ 0.00 | |
| MULTIPLE DEPENDENT CLAIM(S) (if applicable) | | | + **$280.00** | $ 0.00 | |
| **TOTAL OF ABOVE CALCULATIONS =** | | | | $ 890.00 | |
| [ ] Applicant claims small entity status. See 37 CFR 1.27. The fees indicated above are reduced by 1/2. + | | | | $ 0.00 | |
| **SUBTOTAL =** | | | | $ 890.00 | |
| Processing fee of **$130.00** for furnishing the English translation later than [ ] 20 [ ] 30 months from the earliest claimed priority date (37 CFR 1.492(f)). | | | | $ 0.00 | |
| **TOTAL NATIONAL FEE =** | | | | $ 890.00 | |
| Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). **$40.00** per property + | | | | $ 40.00 | |
| **TOTAL FEES ENCLOSED =** | | | | $ 930.00 | |
| | | | | **Amount to be refunded:** | $ |
| | | | | **charged:** | $ |

a. [ ] A check in the amount of $ ______________ to cover the above fees is enclosed.

b. [X] Please charge my Deposit Account No. 13-3848 in the amount of $ 930.00 to cover the above fees. A duplicate copy of this sheet is enclosed.

c. [X] The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 13-3848. A duplicate copy of this sheet is enclosed.

d. [ ] Fees are to be charged to a credit card. **WARNING:** Information on this form may become public. **Credit card information should not be included on this form.** Provide credit card information and authorization on PTO-2038.

**NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137 (a) or (b)) must be filed and granted to restore the application to pending status.**

SEND ALL CORRESPONDENCE TO:

00157

PATENT TRADEMARK OFFICE

Richard E.L. Henderson

SIGNATURE

Richard E.L. Henderson

NAME

31,619

REGISTRATION NUMBER

10/030365

JC10 Rec'd PCT/PTO 02 JAN 2002

PATENT APPLICATION
Mo6888
LeA 33,693

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

| | |
|---|---|
| IN APPLICATION OF | ) PCT/00/EP00/05829 |
| REINHARD LANGER ET AL | ) |
| SERIAL NO.: TO BE ASSIGNED | ) |
| FILED: HEREWITH | ) |
| TITLE: METHOD FOR OXIDATING ORGANIC COMPOUNDS | ) |

**PRELIMINARY AMENDMENT**

Assistant Commissioner for Patents

Washington, D.C. 20231

Sir:

Prior to examination, please amend the application as follows.

"Express Mail" mailing label number ET700176001US

Date of Deposit January 2, 2002

I hereby certify that this paper or fee is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR 1.10 on the date indicated above and is addressed to the Assistant Commissioner of Patents and Trademarks, Washington, D.C. 20231

Donna J. Veatch
(Name of person mailing paper or fee)

Donna J. Veatch
(Signature of person mailing paper or fee)

IN THE SPECIFICATION:

Please replace the title at page 1, line 1, with

-- METHOD FOR OXIDATING ORGANIC COMPOUNDS --

IN THE CLAIMS:

Please replace the heading at page 20, line 1, with --WHAT IS CLAIMED IS:--

Please cancel Claims 1-12 and add Claims 13-25.

--13. A process comprising oxidizing an organic compound with a peroxy-carboxylic acid generated in situ in the presence of an enzyme, wherein the peroxy-carboxylic acid is generated by reacting hydrogen peroxide with (a) a saturated aliphatic carboxylic acid ester of a straight-chain or branched saturated aliphatic carboxylic acid having 1 to 4 carbon atoms and an alcohol having the formula R-OH, wherein R is a straight-chain or branched $C_3$-$C_{18}$-alkyl radical in which the $C_3$-$C_{18}$-alkyl radical is (i) optionally substituted by one or two radicals OR', wherein each R' is independently hydrogen or a $C_2$-$C_4$-acyl radical and/or (ii) optionally interrupted by one or more oxygen atoms, (b) a mixture of a straight-chain or branched saturated aliphatic carboxylic acid having 1 to 4 carbon atoms and an alcohol having the formula R-OH, wherein R is defined as above, or (c) a combination thereof, while removing some or all of the water that is formed and/or introduced during the reaction.

14. The process according to Claim 13 wherein the saturated aliphatic carboxylic acid and/or the saturated aliphatic carboxylic acid part of the saturated aliphatic carboxylic acid ester has 2 or 3 carbon atoms.

15. The process according to Claim 13 wherein the alcohol is an alcohol having the formula R-OH and/or the alcohol part of the saturated aliphatic carboxylic acid ester corresponds to an alcohol having the formula R-OH, wherein R is a straight-chain or branched $C_4$-$C_8$-alkyl radical, a monohydroxyl-substituted $C_3$-$C_6$-alkyl radical, or a $C_3$-$C_6$-alkyl radical substituted by two hydroxyl or O-($C_2$-$C_4$)-acyl radicals.

16. The process according to Claim 13 wherein butyl acetate and/or an acetic acid/butanol mixture is used.

17. The process according to Claim 13 wherein the enzyme is a hydrolase.

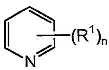
18. The process according to Claim 17 wherein the hydrolase is an esterase, lipase, or protease.

19. The process according to Claim 17 wherein the hydrolase is a lipase obtained from Candida antarctica.

20. The process according to Claim 13 wherein the water that is formed and/or introduced during the reaction is removed until the water content is 0.001 to 10% by weight.

21. The process according to Claim 13 wherein a pyridine is oxidized to a pyridine N-oxide, an olefin is oxidized to an oxirane, a sulfide is oxidized to a sulfoxide and/or sulfone, or a ketone is oxidized to an ester.

22. The process according to Claim 13 wherein a pyridine of formula Ia



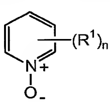
Ia

where

n is an integer from 0 to 5, and

$R^1$ are identical or different and are H, $C_1$-$C_{10}$-alkyl, $C_3$-$C_{10}$-cycloalkyl, $C_6$-$C_{12}$-aryl, OH, $C_1$-$C_{10}$-alkoxy, C(=O)-$C_1$-$C_{10}$-alkyl, C(=O)-O-$C_1$-$C_{10}$-alkyl, CN, $NO_2$, F, Cl, Br, $C(=O)N(R')_2$ in which R' are identical or different and are hydrogen or a $C_1$-$C_{10}$-alkyl radical, or NH-C(=O)R' in which R' are identical or different and are hydrogen or a $C_1$-$C_{10}$-alkyl radical, or any two adjacent $R^1$ together form a $C_2$-$C_{20}$-alkylene or $C_2$-$C_{20}$-alkylidene radical in which each alkylene and alkylidene radical is optionally interrupted once or more than once by O, COO, or CO,

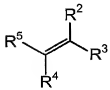
is oxidized to a pyridine N-oxide of formula Ib



Ib

where n and $R^1$ are defined as for formula Ia.

23. The process according to Claim 13 wherein an olefin of formula IIa

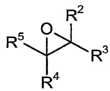


IIa

where

$R^2$, $R^3$, $R^4$, and $R^5$, independently of one another, are H, $C_1$-$C_{10}$-alkyl, $C_3$-$C_{10}$-cycloalkyl, $C_6$-$C_{12}$-aryl, OH, $C_1$-$C_{10}$-alkoxy, C(=O)-$C_1$-$C_{10}$-alkyl, C(=O)-O-$C_1$-$C_{10}$-alkyl, CN, $NO_2$, F, Cl, Br, C(=O)N(R')$_2$ in which R' are identical or different and are hydrogen or a $C_1$-$C_{10}$-alkyl radical, or NH-C(=O)R' in which R' are identical or different and are hydrogen or a $C_1$-$C_{10}$-alkyl radical, or any two adjacent $R^2$, $R^3$, $R^4$, and $R^5$ together form a $C_2$-$C_{20}$-alkylene or $C_2$-$C_{20}$-alkylidene radical in which each alkylene and alkylidene radical is optionally interrupted once or more than once by O, COO, or CO,

is oxidized to an oxirane of formula IIb



IIb

where $R^2$, $R^3$, $R^4$, and $R^5$ are defined as for formula IIa.

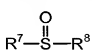
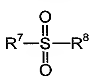
24. The process according to Claim 13 wherein a sulfide of formula IIIa

$R^7$—S—$R^8$ IIIa

where

$R^7$ and $R^8$ are identical or different and are H, $C_1$-$C_{10}$-alkyl, $C_3$-$C_{10}$-cycloalkyl, or $C_6$-$C_{12}$-aryl, or together form a $C_2$-$C_{20}$-alkylene or $C_2$-$C_{20}$-alkylidene radical in which each alkylene and alkylidene radical is optionally interrupted once or more than once by O, COO, or CO,

is oxidized to a sulfoxide of formula IIIb and/or a sulfone of formula IIIc

 and/or 

IIIb IIIc

where $R^7$ and $R^8$ are defined as for formula IIIa.

25. The process according to Claim 13 wherein a ketone of formula IVa

$$R^9-\overset{\overset{\displaystyle O}{\|}}{C}-R^{10} \qquad \text{IVa}$$

where

$R^9$ and $R^{10}$ are identical or different and are H, $C_1$-$C_{10}$-alkyl, $C_3$-$C_{10}$-cycloalkyl, or $C_6$-$C_{12}$-aryl, or together form a $C_2$-$C_{20}$-alkylene or $C_2$-$C_{20}$-alkylidene radical in which each alkylene and alkylidene radical is optionally interrupted once or more than once by O, COO, or CO,

is oxidized to an ester of formula IVb

$$R^9-\overset{\overset{\displaystyle O}{\|}}{C}-OR^{10} \qquad \text{IVb}$$

where $R^9$ and $R^{10}$ are defined as for formula IVa.--

IN THE ABSTRACT:

Please add an Abstract as new page 25 to read as follows:

--METHOD FOR OXIDATING ORGANIC COMPOUNDS

ABSTRACT OF THE DISCLOSURE

The invention relates to a method for oxidizing organic compounds with peroxy-carboxylic acids that are produced in situ in the presence of enzymes by reacting hydrogen peroxide with saturated aliphatic carboxylic acid esters of short-chain carboxylic acids and long-chain alcohols and/or mixtures of corresponding carboxylic acids and alcohols while partly or wholly removing any water produced and/or added during the reaction.--

## REMARKS

Applicants hereby offer preliminary amendments to the present application to place the application in better form for allowance.

Applicants have canceled Claims 1-12 in favor of replacement Claims 13-25 to correct certain informalities (including avoidance of multiple dependencies and removal of preferences or addition of new claims directed to such preferences) and to clarify the intended meaning of the claims. Claim 1 has been replaced by replacement Claim 13, which, although written using a different format, is directed to exactly the same subject matter as Claim 1. Applicants respectfully submit that the claims are fully supported in the specification.

Applicants have amended the specification to change the title to correspond to the English version of the title appearing on the International Application and to capitalize all letters in the title. Applicants submit that these amendments serve only to clarify their application and do not alter the scope of their disclosure.

Applicants have added an Abstract that summarizes the subject matter of their invention. A copy of the new Abstract is separately attached.

In view of the preceding amendments and remarks, allowance of the claims is respectfully requested.

Respectfully submitted,

By Richard E L Henderson

Richard E. L. Henderson
Attorney for Applicants
Reg. No. 31,619

Bayer Corporation
100 Bayer Road
Pittsburgh, Pennsylvania 15205-9741
PHONE: (412) 777-8341
FACSIMILE PHONE NUMBER:
412-777-8363

s/rmc/relh0074

## ANNOTATED VERSION OF AMENDMENTS

**IN THE SPECIFICATION:**

The title at page 1, line 1, has been changed from "**Process for the oxidation of organic compounds**" to

--METHOD FOR OXIDATING ORGANIC COMPOUNDS--

**IN THE CLAIMS:**

The heading for the claims at page 20, line 1, has been changed from "**Claims:**" to --WHAT IS CLAIMED IS:--

As explicitly set forth in 37 C.F.R. 1.121(c)(1)(ii), an annotated version does not need to be supplied for an added claim or a canceled claim as long as it is stated that a particular claim has been added or canceled. Here, Claims 1-12 have been canceled and Claims 13-25 have been added.

**IN THE ABSTRACT:**

An Abstract has been added as new page 25 as follows:

--METHOD FOR OXIDATING ORGANIC COMPOUNDS

ABSTRACT OF THE DISCLOSURE

The invention relates to a method for oxidizing organic compounds with peroxy-carboxylic acids that are produced in situ in the presence of enzymes by reacting hydrogen peroxide with saturated aliphatic carboxylic acid esters of short-chain carboxylic acids and long-chain alcohols and/or mixtures of corresponding carboxylic acids and alcohols while partly or wholly removing any water produced and/or added during the reaction.--

# METHOD FOR OXIDATING ORGANIC COMPOUNDS

## ABSTRACT OF THE DISCLOSURE

The invention relates to a method for oxidizing organic compounds with peroxycarboxylic acids that are produced in situ in the presence of enzymes by reacting hydrogen peroxide with saturated aliphatic carboxylic acid esters of short-chain carboxylic acids and long-chain alcohols and/or mixtures of corresponding carboxylic acids and alcohols while partly or wholly removing any water produced and/or added during the reaction.

**Process for the oxidation of organic compounds**

The invention relates to a process for the oxidation of organic compounds with peroxycarboxylic acids which are generated in situ with hydrogen peroxide from saturated aliphatic carboxylic esters and/or mixtures of the corresponding carboxylic acids and alcohols in the presence of enzymes as catalysts.

The oxidation of organic compounds using peroxycarboxylic acids which are prepared in situ from carboxylic acids with hydrogen peroxide in the presence of enzyme catalysts is known in principle. Examples of reactions in which peroxycarboxylic acids are used as oxidizing agents are:

- the epoxidation of olefins
- the Baeyer-Villiger oxidation of ketones to esters
- the oxidation of amines to amine oxides, nitroso and nitro compounds
- the oxidation of aliphatic aldehydes to carboxylic acids
- the oxidation of aromatic aldehydes to phenols.

A favorable aspect of using peroxycarboxylic acids in such oxidation reactions is that they have a markedly greater and more selective oxidizing power than hydrogen peroxide itself. Although some peroxycarboxylic acids are useful and commercially available reagents, their use is limited due to their relatively high costs and the risks (in particular the danger of explosion) which are associated with the handling of the reagents, particularly on an industrial scale. By using enzymes for the preparation of the peroxycarboxylic acids it is possible to choose significantly milder reaction conditions. This reduces, primarily, the risks which exist when handling peroxycarboxylic acids. In addition, it becomes possible to also react thermally sensitive carboxylic acids to the corresponding peroxycarboxylic acids.

Thus, Tetrahedron 48 (1992), 4587-92 describes the lipase-catalyzed preparation of long-chain $C_6$-$C_{16}$-peroxycarboxylic acids by reacting the corresponding carboxylic

acids with hydrogen peroxide, and the in situ use of these peroxycarboxylic acids for the oxidation of alkenes and sulfides. This in situ preparation of the peroxycarboxylic acids, and the oxidation of the alkenes and sulfides is generally carried out either in a two-phase system of an organic solvent and water, or else only in the presence of water without further solvent.

WO-A-91/04333 likewise describes a process for the preparation of peroxycarboxylic acids by reacting the corresponding carboxylic acids with hydrogen peroxide in the presence of enzymes as catalysts. The process permits the preparation of peroxycarboxylic acids RCOOOH, where R is an organic radical, in particular a linear or branched, saturated or unsaturated alkyl radical, an aryl radical or an alkylaryl radical, each of which may be substituted by a very wide variety of groups and radicals. The radical R can, for example, be a $C_1$-$C_{30}$-alkyl radical. The clear emphasis of WO-A-91/04333 is on the longer-chain peroxycarboxylic acids with $C_6$-$C_{18}$-alkyl radicals prepared in the examples. The enzymes used are preferably hydrolases, such as proteases or lipases. The preparation of the peroxycarboxylic acids can be undertaken in the solution of the parent carboxylic acid itself or else in a solvent. The solvents mentioned are, explicitly, water, aqueous buffer solutions, or else organic solvents, e.g. hydrocarbons, such as hexane, cyclohexane, heptane, benzene, toluene, methylene chloride, hexachloroethane, acetonitrile, DMF, dioxane or THF.

WO-A-91/04333 also describes the oxidation of organic compounds using the in situ prepared peroxycarboxylic acids. The experiments describe the oxidation of alkenes to oxiranes, of ketones to esters and of sulfides to sulfoxides in the presence of hydrogen peroxide and enzymes, and the longer-chain carboxylic acids octanoic acid or myristic acid. The hydrogen peroxide requirement here, being 1.5 to 5 mol per mole of starting material, is considerably greater than the stoichiometric amount, and in many cases, highly concentrated 60% strength hydrogen peroxide has to be used. The immobilized enzyme is also used in very large amounts. Despite this, for long

reaction times between 4 and 24 h, the conversions and yields achieved are generally incomplete, and at times even as low as approximately 10 to 60%.

WO-A-98/36058 describes the continuous removal of water of reaction which is formed during enzyme-catalyzed reactions, by pressure permeation on a special nonporous membrane. The enzyme catalyst is also simultaneously fixed to this nonporous membrane. Reactions catalyzed in this way are the etherification of monosaccharides to give polysaccharides in the presence of carbohydrases, and also the esterification of carboxylic acids with alcohols in the presence of lipases and the formation of amides from amino acids in the presence of proteases. The membrane systems described are complicated and are not used for the preparation of peroxycarboxylic acids or the oxidation of organic compounds.

EP-A-0 310 952 describes a process for the preparation of dilute aqueous peroxycarboxylic acid solutions for use as bleaches and disinfectants. The process involves the reaction of carboxylic esters with hydrogen peroxide in the presence of hydrolases. To achieve a sensible selectivity here, it is essential that the hydrolases are proteases and, in some instances, that the process is carried out in the presence of surfactants and under alkaline conditions. The starting materials used for the percarboxylic acids are esters of monocarboxylic acids. In principle, it is possible to use esters of monocarboxylic acids having 1 to 24 carbon atoms in the acid moiety, where the concentration of the carboxylic esters is preferably between 1 and 10% by weight, based on the total solution. The emphasis of EP-A-0 310 952 is on longer-chain monocarboxylic acids having 4 to 10 carbon atoms in the acid moiety and on short-chain alcohol radicals having 1 to 4 carbon atoms. Particular attention is directed to the preparation of percarboxylic acids having 8 carbon atoms in the acid moiety since such percarboxylic acids have particularly favorable properties for the intended use as bleaches and disinfectants.

Also known, from DE-A-2 240 605, are compositions which are used as bleaches in the washing of textiles in an aqueous medium for domestic or industrial purposes.

These compositions comprise acylalkyl esters having in each case 1 to 10 carbon atoms in the acid and alcohol radical, and a hydrolase. Increasing the temperature in the wash liquor results in the formation of the corresponding peracids which, because of their bleaching action, remove a wide spectrum of stains and soilings. EP-A-0 268 456 and EP-A-0 253 487 also describe similar bleach compositions for the washing of textiles.

DE-197 38 442-A1 also describes the preparation of percarbonic half-esters of the formula ROC(O)OOH by catalytic perhydrolysis of carbonic diesters with hydrogen peroxide. The resulting percarbonic half-esters can be used in situ as oxidizing agents.

From Proc. World Congr. Int. Soc. Fat Res., 21st (1996), 3, 469-471, it is likewise known to carry out the oxidation of alkenes in the presence of peroxycarboxylic acids which are prepared in situ by reacting carboxylic acids and hydrogen peroxide. A broad spectrum of carboxylic acids is used; particular attention is here again on the long-chain carboxylic acids/fatty acids having up to 22 carbon atoms since these lead to yields in the region of 60% in the oxidation of 1-octene. The use of short-chain carboxylic acids, such as propionic acid or isobutyric acid, produces, by contrast, yields of only 41% or even only 25% of 1,2-epoxyoctane. Also described is the use of esters of long-chain carboxylic acids with short-chain alcohols, which are cleaved in the presence of lipases under action of the hydrogen peroxide likewise to give peroxycarboxylic acids, and then catalyze the alkene oxidation. In the oxidation of 1-octene, these carboxylic esters, however, always lead to considerably poorer yields than the corresponding free carboxylic acids: for example, the use of the methyl, butyl or vinyl ester of dodecanoic acid leads to yields of only between 13 and 33%, while the free acid produces a yield of 59%. Against this backdrop of considerably poorer yields, the authors give as the sole reason for using carboxylic esters the advantage that less concentrated hydrogen peroxide solutions can be used. Only the use of the trifluoroethyl esters of dodecanoic acid leads to a good yield, comparable

with the free dodecanoic acid, of 62%, which the authors, however, attribute to the trifluoroethyl radical as a good leaving group.

Since oxidation reactions are some of the basic and most common reactions of organic chemistry, the object of the present invention was to provide an oxidation process which allows relatively high conversions of starting materials to be achieved with simple technical measures and under mild reaction conditions.

The invention provides a process for the oxidation of organic compounds with peroxycarboxylic acids, which are generated in situ in the presence of enzymes by reacting hydrogen peroxide with saturated aliphatic carboxylic esters and/or mixtures of the corresponding carboxylic acids and alcohols, characterized in that the saturated aliphatic carboxylic acids are straight-chain or branched and have 1 to 4 carbon atoms, and the alcohols have the formula

R-OH

where

R is a straight-chain or branched $C_3$-$C_{18}$-alkyl radical which is optionally substituted by one or two radicals OR', where R', independently of one another, are hydrogen or a $C_2$-$C_4$-acyl radical, and whose alkyl chain is optionally interrupted by one or more oxygen atoms, and

that some or all of the water which is formed and/or introduced during the reaction is removed.

In the process according to the invention, saturated aliphatic carboxylic esters and/or mixtures of the corresponding carboxylic acids and alcohols are used for the in situ preparation of the peroxycarboxylic esters, where the carboxylic acids have 1 to 4 carbon atoms, preferably 2 or 3 carbon atoms.

In the case of the alcohols of the formula ROH, preference is given to those in which R is a linear or branched $C_4$-$C_8$-alkyl radical or a monohydroxyl-substituted $C_3$-$C_6$-alkyl radical, in particular an $\omega$-hydroxy-$C_3$-$C_6$-alkyl radical. Also suitable are those alcohols in which R is a $C_3$-$C_6$-alkyl radical which is substituted by one or two hydroxyl or O-($C_2$-$C_4$)-acyl radicals. Particular preference is given here to a glycerol radical in which 1 or 2 OH groups are esterified by an O-($C_2$-$C_4$)-acyl radical. In the process according to the invention, particular preference is given to using butyl acetate as aliphatic carboxylic ester and/or acetic acid/butanol mixtures.

Enzymes which can be used in the process according to the invention are hydrolases, such as esterases or proteases. Preference is given to using lipases, proteases or peptidases. The suitability of a given enzyme for use in the present process can be readily tested by exposing a carboxylic ester substrate in the presence of the enzyme to hydrogen peroxide or to a hydrogen peroxide precursor, and monitoring the generation of peroxycarboxylic acid from the reaction. The enzyme can be used as it is, as a solution, in lyophilized form, in chemically modified form, or else immobilized on a carrier, in order to increase its stability and its activity toward the substrate in question. Preference is given to using enzymes which are readily handlable and have been stabilized by immobilization on carriers.

Lipases which can be used in the present process may be microbial lipases which are produced, for example, from strains of Aspergillus, Enterobacterium, Chromobacterium, Geotricium or Penicillium. Preferred lipases for use according to the invention are those produced by species of Mucor, Humicola, Pseudomonas or Candida.

Particularly preferred lipases are those produced by the following microorganism strains, which have all been deposited in the Deutsche Sammlung von Mikroorganismen in accordance with the provisions of the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure:

Candida antarctica, deposited on September 29, 1986, with the number DSM 3855, and on December 8, 1986, with the numbers DSM 3908 and DSM 3909.

Pseudomonas cephacia, deposited on January 30, 1987, with the number 3959.

Humicola lanuginosa, deposited on August 13, 1986 and on May 4, 1987 with the deposit numbers 3819 and 4109, respectively.

Humicola brevispora, deposited on May 4, 1987, with the deposit number DSM 4110.

Humicola brevis var. thermoidea, deposited on May 4, 1987, with the deposit number DSM 4111, and

Humicola insolens, deposited on October 1, 1981, with the deposit number DSM 1800.

Currently preferred lipases are those produced by Candida antarctica, DSM 3855, DSM 3908 and DSM 3909. These enzymes can be prepared using the process disclosed in WO 88/02775. The Candida strains in question can be cultivated under aerobic conditions in a nutrient medium which contains assimilable carbon and nitrogen sources and also essential minerals, trace elements etc., the medium being composed according to established practice. After cultivation, liquid enzyme concentrate can be prepared by removing insoluble materials, e.g. by filtration or centrifugation, after which the culture broth can be concentrated by evaporation or reverse osmosis. Solid enzyme preparations can be prepared from the concentrate by precipitation with salts or water-miscible solvents, e.g. ethanol, or by drying, such as, for example, spray-drying, in accordance with well known processes.

Additional lipases can be obtained from the following strains which are available to the public without limitation from the Centraalbureau voor Schimmelculturen (CBS),

from the American Type Culture Collection (ATCC), from the Agricultural Research Culture Collection (NRRL) and from the Institute of Fermentation, Osaka (IFO), having the following deposit numbers: Candida antarctica, CBS 5955, ATCC 34888, NRRL Y-8295, CBS 6678, ATCC 28323, CBS 6821 and NRRL Y-7954; Candida tsukubaensis, CBS 6389, ATCC 24555 and NRRL Y-7795; Candida auriculariae, CBS 6379, ATTC 24121 and IFO 1580; Candida humicola, CBS 571, ATCC 14438, IFO 0760, CBS 2041, ATTC 9949, NRRL Y-1266, IFO 0753 and IFO 1527; and Candida foliorum, CBS 5234 and ATCC 18820.

It is known to prepare lipase by recombinant DNA techniques, cf. e.g. EP-A-0 238 023. Recombinant lipases can also be used for the present purpose.

Where used in the process of the invention, the enzyme can be present in a soluble state. It is, however, preferred to immobilize the enzyme in order to facilitate isolation of the peroxycarboxylic acids prepared using the present process. Immobilization processes are well known and include crosslinking of cell homogenates, covalent coupling to insoluble organic or inorganic carriers, inclusion in gels and adsorption to ion exchange resins or other adsorbing materials. Application to a particulate carrier can likewise be used (e.g. A.R. Macrae and R.C. Hammond, Biotechnology and Genetic Engineering Reviews, 3, 1985, p. 193). Suitable carrier materials for the immobilized enzyme are, for example, plastics (e.g. polypropylene, polystyrene, polyvinyl chloride, polyurethane, latex, nylon, Teflon, Dacron, polyvinyl acetate, polyvinyl alcohol or any suitable copolymer thereof), polysaccharides (e.g. agarose or dextran). Ion exchanger resins (both cation and anion exchange resins), silicon polymers (e.g. siloxane) or silicates (e.g. glass).

It is preferred to immobilize the enzyme on an ion exchange resin by adsorbing the enzyme to the resin or by crosslinking it with the resin using gluteraldehyde or another crosslinking agent in a manner known per se. A particularly preferred resin is a weakly basic anion exchange resin, which may be a resin of the polystyrene, acrylic or phenol-formaldehyde type. Examples of commercially available resins of the

polyacrylic type are Lewatit® E 1999/85 (registered trademark of Bayer, Federal Republic of Germany) and Duolite® ES-568 (registered trademark of Rohm & Haas, Federal Republic of Germany). Immobilization of enzymes on this type of resin can be carried out as in EP-A-0 140 542. Immobilization on resins of the phenyl-formaldehyde type can be carried out as in DK 85/878. One example of a commercially available resin of the acrylic type is Lewatit® E 2001/85 (registered trademark of Bayer, Federal Republic of Germany).

Another suitable material for immobilizing enzymes is an inorganic carrier, such as, for example, a silicate. The enzyme can be bound to the carrier by adsorption or by covalent coupling.

It is also possible to use mixtures of enzymes.

The process according to the invention is carried out at temperatures of from 10 to 110°C, preferably 20 to 90°C, particularly preferably 40 to 60°C.

The hydrogen peroxide used as oxidizing agent is usually used in the form of a 10 to 70% strength, preferably in the form of a 20 to 40% strength, aqueous solution, meaning that 1 to 100 mol, preferably 1.1 to 10 mol and in particular 1.2 to 2 mol, of hydrogen peroxide are present per oxidation equivalent of organic compound. The metered addition can either take place discontinuously in the form of a single addition, or in two or more portions, or else continuously at a certain desired rate. Alternatively, it is possible to use a hydrogen peroxide precursor which liberates hydrogen peroxide in situ under the reaction conditions, e.g. percarbonates or perborates each in the form of their alkali metal or alkaline earth metal salts.

An essential feature of the process according to the invention consists in removing the water which is formed in the process according to the invention and/or is introduced to the reaction system, from the reaction system. This water can be separated off, firstly, directly in the reactor during the reaction, i.e. by evaporation,

optionally by pervaporation or vapor pervaporation. Preference is given to carrying out a simple distillation. Alternatively to this, a partial stream of the liquid reaction mixture which is in contact with the enzyme can be removed from the reactor and then, spatially separate from the enzyme, the water outside of the reactor can be removed, for example, by evaporation and the reaction stream freed from water can be reintroduced. It has proven successful to remove the water until the water content in the reaction mixture is 0.001 to 10% by weight, preferably 0.01 to 3% by weight and in particular 0.1 to 2% by weight.

If the water is separated off from the reaction mixture spatially separate from the enzyme, then during the water removal, temperatures in the range from 50 to 200°C, preferably 80 to 160°C are set.

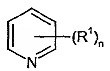
The water is removed at a pressure in the range from 0.001 to 10 bar, preferably 0.01 to 1 bar.

In the process according to the invention, the carboxylic ester generally also serves as solvent. It has, however, also proven successful to additionally use one or more inert organic solvents. Some preferred organic solvents are hydrocarbons, such as hexane, cyclohexane, heptane, benzene, toluene, the isomeric xylenes and mixtures thereof, chlorobenzene, dichlorobenzene, methylene chloride, hexachloroethane, acetonitrile, dimethylformamide, dioxane and tetrahydrofuran. The use of such a solvent is particularly advantageous if it forms an azeotrope with the water to be removed, thus simplifying removal of the water. Particular preference is given to the use of such solvents which form a heteroazeotrope with water so that simple recycling of the solvent is ensured. As an alternative to adding organic solvents, the compound to be oxidized can also simultaneously serve as solvent.

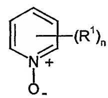
The reaction times are usually 0.5 to 24 hours, preferably 2 to 12 hours and particularly preferably 4 to 8 hours. The water can be removed throughout the entire reaction period or in certain time periods.

The process according to the invention is particularly suitable for oxidizing pyridines to pyridine N-oxides, olefins to oxiranes, hydrosulfides to disulfides, sulfides to sulfoxides and sulfones and ketones to esters. Particular preference is given to oxidizing pyridines and olefins, and very particularly preferably pyridines are converted into the corresponding N-oxides.

In the process according to the invention, pyridines of the formula Ia can be oxidized to pyridine N-oxides of the formula Ib,



Ia



Ib

where

n is an integer from 0 to 5,

$R^1$ are identical or different and are H, $C_1$-$C_{10}$-alkyl, $C_3$-$C_{10}$-cycloalkyl, $C_6$-$C_{12}$-aryl, OH, $C_1$-$C_{10}$-alkoxy, C(=O)-$C_1$-$C_{10}$-alkyl, C(=O)-O-$C_1$-$C_{10}$-alkyl, CN, $NO_2$, F, Cl, Br, C(=O)N(R')$_2$, where R' are identical or different and are hydrogen or a $C_1$-$C_{10}$-alkyl radical, NH-C(=O)R', where R' has the meaning given above, or else in each case two adjacent substituents $R^1$ together form a $C_2$-$C_{20}$-alkylene or $C_2$-$C_{20}$-alkylidene radical, where these alkylene and alkylidene radicals may be interrupted once or more than once by O, COO or CO.

Preference is given to using pyridines of the formula Ia in which

n is an integer from 0 to 3 and, independently thereof,

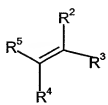
$R^1$ are identical or different and H, $C_1$-$C_6$-alkyl, $C_3$-$C_6$-cycloalkyl, phenyl, OH, $C_1$-$C_6$-alkoxy, C(=O)-$C_1$-$C_6$-alkyl, C(=O)-O-$C_1$-$C_6$-alkyl, CN, $NO_2$, F, Cl, Br, C(=O)N(R')$_2$, where R' are identical or different and are hydrogen or a $C_1$-$C_6$-alkyl radical, NH-C(=O)R', where R' has the meaning given above, or else in each case two adjacent substituents $R^1$ can together form a $C_3$-$C_{10}$-alkylene or $C_3$-$C_{10}$-alkylidene radical, where these alkylene and alkylidene radicals may be interrupted once or more than once by O, COO or CO.

Particular preference is given to using pyridines of the formula Ia in which

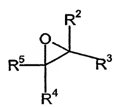
n is an integer from 1 to 3 and, independently thereof,

$R^1$ are identical or different and are $CH_3$, $NO_2$ or Cl, or two adjacent substituents $R^1$, including the two carbon atoms of the pyridine ring, form a fused-on phenyl or naphthyl radical.

Using the process according to the invention, it is also possible to oxidize olefins of the formula IIa to oxiranes of the formula IIb,



IIa



IIb

where

$R^2$, $R^3$, $R^4$ and $R^5$, independently of one another, are H, $C_1$-$C_{10}$-alkyl, $C_3$-$C_{10}$-cycloalkyl, $C_6$-$C_{12}$-aryl, OH, $C_1$-$C_{10}$-alkoxy, C(=O)-$C_1$-$C_{10}$-alkyl, C(=O)-O-$C_1$-$C_{10}$-alkyl, CN, $NO_2$, F, Cl, Br, C(=O)N(R')$_2$, where R' are identical or different and are hydrogen or a $C_1$-$C_{10}$-alkyl radical, NH-C(=O)R', where R' has the meaning given above, or else in each case two adjacent radicals from the group of $R^{2-5}$ together form a $C_2$-$C_{20}$-alkylene or

$C_2$-$C_{20}$-alkylidene radical, where these alkylene and alkylidene radicals may be interrupted once or more than once by O, COO or CO.

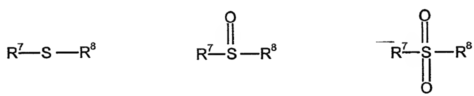
Preference is given to using olefins of the formula IIa in which

$R^2$, $R^3$, $R^4$ and $R^5$ independently of one another, are H, $C_1$-$C_6$-alkyl, $C_3$-$C_6$-cycloalkyl, phenyl, OH, $C_1$-$C_6$-alkoxy, C(=O)-$C_1$-$C_6$-alkyl, C(=O)-O-$C_1$-$C_6$-alkyl, CN, $NO_2$, F, Cl, Br, C(=O)N(R')$_2$, where R' are identical or different and are hydrogen or a $C_1$-$C_6$-alkyl radical, NH-C(=O)R', where R' has the meaning given above, or else in each case two adjacent radicals from the group of $R^{2-5}$ together form a $C_3$-$C_{10}$-alkylene or $C_3$-$C_{10}$-alkylidene radical, where these alkylene and alkylidene radicals may be interrupted once or more than once by O, COO or CO.

Particular preference is given to using olefins of the formula IIa in which

$R^2$, $R^3$, $R^4$ and $R^5$, independently of one another, are $CH_3$, $NO_2$ or Cl or in each case two adjacent radicals from the group of $R^{2-5}$ including the two olefin carbon atoms form a phenyl or naphthyl ring.

With the process according to the invention, the oxidation of sulfides of the formula IIIa to sulfoxides of the formula IIIb and to sulfones of the formula IIIc is also possible,



IIIa IIIb IIIc

where

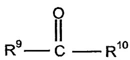
$R^7$ and $R^8$ are identical or different and are H, $C_1$-$C_{10}$-alkyl, $C_3$-$C_{10}$-cycloalkyl or $C_6$-$C_{12}$-aryl, or else both substituents $R^7$ and $R^8$ together form a $C_2$-$C_{20}$-

alkylene or $C_2$-$C_{20}$-alkylidene radical, where these alkylene and alkylidene radicals may be interrupted once or more than once by O, COO or CO.

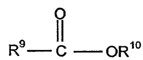
Preference is given to using sulfides of the formula IIIa in which

$R^7$ and $R^8$ are identical or different and are H, $C_1$-$C_6$-alkyl, $C_3$-$C_6$-cycloalkyl, or are phenyl, or else both substituents $R^7$ and $R^8$ together form a $C_4$-$C_{10}$-alkylene or $C_4$-$C_{10}$-alkylidene radical, where these alkylene and alkylidene radicals can be interrupted once or more than once by O, COO or CO.

With the process according to the invention it is also possible to oxidize ketones of the formula IVa to esters of the formula IVb,



IVa



IVb

where

$R^9$ and $R^{10}$ are identical or different and are H, $C_1$-$C_{10}$-alkyl, $C_3$-$C_{10}$-cycloalkyl or $C_6$-$C_{12}$-aryl, or else the two substituents $R^9$ and $R^{10}$ together form a $C_2$-$C_{20}$-alkylene or $C_2$-$C_{20}$-alkylidene radical, where these alkylene and alkylidene radicals may be interrupted once or more than once by O, COO or CO.

Preference is given to using ketones of the formula IVa in which

$R^9$ and $R^{10}$ are identical or different and are H, $C_1$-$C_6$-alkyl, $C_3$-$C_6$-cycloalkyl, or are phenyl, or else the two substituents $R^9$ and $R^{10}$ together form a $C_3$-$C_{10}$-alkylene or $C_3$-$C_{10}$-alkylidene radical, where these alkylene and alkylidene radicals may be interrupted once or more than once by O, COO or CO.

In the process according to the invention, the molar ratio between the organic compound to be oxidized and the carboxylic ester or the carboxylic acid is 0.1:1 to 1000:1, preferably 0.5:1 to 500:1.

Suitable reactors for the process according to the invention are all reactors for the reaction of liquid reaction mixtures, as are known from the prior art. In the preferred case of the use of enzymes immobilized on carriers, the catalyst particles are used floating in the liquid, or can be in the form of solid stationary catalyst beds through which the reaction mixture flows.

Suitable reactors are, for example, stirred-tank reactors, preferably those with column and water separator, and also bubble columns, loop reactors with or without stationary catalyst bed, tubular reactors and tube-bundle reactors with stationary catalyst bed.

The process according to the invention is characterized by the fact that the oxidation of a wide spectrum of organic compounds is possible using only slight excesses of hydrogen peroxide and small amounts of enzyme catalyst. Also worthy of emphasis are the mild reaction conditions, the short reaction times and the high conversions which can be achieved.

## Examples

### Description of the experimental set-up

All reactions are carried out in a 500 ml three-necked flask equipped with a water separator, a stirrer with magnetic coupling and a dropping funnel. A vacuum pump is attached via the condenser of the water separator.

All experiments are evaluated using gas chromatography or via HPLC with regard to conversion and the selectivity using methods calibrated against pure substances of the starting materials and end products.

### Example 1a

**Oxidation of lutidine to lutidine N-oxide**

26.8 g of lutidine and 1 g of Novozym 435® (registered trademark of Novo Nordisk) are introduced into the above-described experimental apparatus together with 400 ml of butyl acetate. With stirring at 45°C and a reduced pressure of 40 mbar, 30 g of hydrogen peroxide in the form of a 35% strength aqueous solution are added dropwise over the course of 2 hours. The mixture is then after-stirred for 4 hours at 45°C. Throughout the entire time, the water liberated during the reaction and introduced into the reaction is continuously separated off via the water separator. Lutidine is converted to lutidine N-oxide with a conversion of 100% and a selectivity of 96%.

**Example 1b**

**(Comparative example to example 1a without water removal)**

26.8 g of lutidine and 2.6 g of Novozym 435® are introduced into the above-described experimental apparatus together with 400 ml of butyl acetate. With stirring at 45°C, 34 g of hydrogen peroxide in the form of a 35% strength aqueous solution are added dropwise over the course of 2 hours. The mixture is then after-stirred for 4 hours at 45°C. Lutidine is converted to lutidine N-oxide with a conversion of 62% and a selectivity of 95%.

Despite a 2.6-fold amount of catalyst, only a very much lower conversion is achieved in the same reaction time relative to example 1a, which is carried out under conditions according to the invention.

**Example 2**

**Oxidation of 4-cyanopyridine to 4-cyanopyridine N-oxide**

26.0 g of 4-cyanopyridine and 1 g of Novozym 435® are introduced into the above-described experimental apparatus together with 400 ml of butyl acetate. With stirring at 45°C and a reduced pressure of 40 mbar, 30 g of hydrogen peroxide in the form of a 35% strength aqueous solution are added dropwise over the course of 2 hours. The mixture is then after-stirred for 3 hours at 45°C. Throughout the entire time, the water liberated during the reaction and introduced into the reaction is continuously separated off via the water separator. 4-Cyanopyridine is converted to 4-cyanopyridine N-oxide with a conversion of 67% and a selectivity of 95%.

**Example 3**

**Oxidation of cyclohexene to cyclohexene oxide**

20.6 g of cyclohexene and 1 g of Novozym 435® are introduced into the above-described experimental apparatus together with 400 ml of butyl acetate. With stirring at 45°C and a reduced pressure of 70 mbar, 30 g of hydrogen peroxide in the form of a 35% strength aqueous solution are added dropwise over the course of 2 hours. The mixture is then after-stirred for 3 hours at 48°C. Throughout the entire time, the water which is liberated during the reaction and introduced into the reaction is continuously separated off via the water separator. Cyclohexene is converted to cyclohexene oxide with a conversion of 100% and a selectivity of 97%.

**Example 4**

**Oxidation of styrene to styrene oxide**

26.3 g of styrene and 1 g of Novozym 435® are initially introduced into the above-described experimental apparatus together with 400 ml of butyl acetate. With stirring at 45°C and a reduced pressure of 40 mbar, 30 g of hydrogen peroxide in the form of a 35% strength aqueous solution are added dropwise over the course of 2 hours. The mixture is then after-stirred for 3 hours at 45°C. Throughout the entire time, the water which is liberated during the reaction and introduced into the reaction is continuously separated off via the water separator. Styrene is converted to styrene oxide with a conversion of 70% and a selectivity of 99%.

## Example 5

**Oxidation of cyclohexanone to caprolactone**

24.6 g of cyclohexanone and 1 g of Novozym 435® are introduced into the above-described experimental apparatus together with 400 ml of butyl acetate. With stirring at 45°C and a reduced pressure of 40 mbar, 30 g of hydrogen peroxide in the form of a 35% strength aqueous solution are added dropwise over the course of 2 hours. The mixture is then after-stirred for 4 hours at 40°C. Throughout the entire time, the water which is liberated during the reaction and introduced into the reaction is separated off continuously via the water separator. Cyclohexanone is converted to caprolactone with a conversion of 45% and a selectivity of 82%.

## Example 6

**Oxidation of thioanisole to methyl phenyl sulfoxide**

18.8 g of thioanisole and 1 g of Novozym 435® are introduced into the above-described experimental apparatus together with 400 ml of butyl acetate. With stirring at 45°C and a reduced pressure of 40 mbar, 18.5 g of hydrogen peroxide in the form of a 35% strength aqueous solution are added dropwise over the course of 2 hours. The mixture is then after-stirred for 4 hours at 40°C. Throughout the entire time, the water which is liberated during the reaction and introduced into the reaction is continuously separated off via the water separator. Thioanisole is converted to methyl phenyl sulfoxide with a conversion of 93% and a selectivity of 93%.

**Claims:**

1. A process for the oxidation of organic compounds with peroxycarboxylic acids, which are generated in situ in the presence of enzymes by reacting hydrogen peroxide with saturated aliphatic carboxylic esters and/or mixtures of the corresponding carboxylic acids and alcohols, characterized in that the saturated aliphatic carboxylic acids are straight-chain or branched and have 1 to 4 carbon atoms, and the alcohols have the formula

R-OH

where

R is a straight-chain or branched $C_3$-$C_{18}$-alkyl radical which is optionally substituted by one or two radicals OR', where R', independently of one another, are hydrogen or a $C_2$-$C_4$-acyl radical, and whose $C_3$-$C_{18}$-alkyl chain is optionally interrupted by one or more oxygen atoms, and

that some or all of the water which is formed and/or introduced during the reaction is removed.

2. The process as claimed in claim 1, characterized in that saturated aliphatic carboxylic esters and/or mixtures of the corresponding carboxylic acids and alcohols are used in which the carboxylic acids have 2 or 3 carbon atoms.

3. The process as claimed in claim 1 or 2, characterized in that saturated aliphatic carboxylic esters and/or mixtures of the corresponding carboxylic acids and alcohols are used in which

R is a straight-chain or branched $C_4$-$C_8$-alkyl radical, a monohydroxyl-substituted $C_3$-$C_6$-alkyl radical, in particular an $\omega$-hydroxyl-$C_3$-$C_6$-alkyl radical, or a $C_3$-$C_6$-alkyl radical which is substituted by two hydroxyl or O-($C_2$-$C_4$)-acyl radicals.

4. The process as claimed in claim 3, characterized in that butyl acetate and/or acetic acid/butanol mixtures are used.

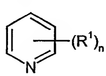
5. The process as claimed in one or more of claims 1 to 4, characterized in that the enzymes used are hydrolases, preferably esterases, lipases or proteases.

6. The process as claimed in claim 5, characterized in that the enzyme used is Candida antarctica.

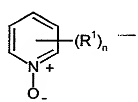
7. The process as claimed in one or more of claims 1 to 7, characterized in that the water which is formed during the reaction and/or introduced into the reaction system is removed from the reaction system such that the water content of the reaction system is 0.001 to 10% by weight, preferably 0.01 to 3% by weight and in particular 0.1 to 2% by weight.

8. The process as claimed in one or more of claims 1 to 6, characterized in that pyridines are oxidized to pyridine N-oxides, olefins are oxidized to oxiranes, sulfides are oxidized to sulfoxides and sulfones or ketones are oxidized to esters.

9. The process as claimed in claim 8, characterized in that pyridines of the formula Ia are oxidized to pyridine N-oxides of the formula Ib,



Ia



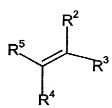
Ib

where

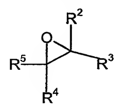
n is an integer from 0 to 5, preferably 0 to 3 and in particular 1 to 3,

$R^1$ are identical or different and are H, $C_1$-$C_{10}$-alkyl, preferably $C_1$-$C_6$-alkyl, in particular $CH_3$, $C_3$-$C_{10}$-cycloalkyl, preferably $C_3$-$C_6$-cycloalkyl, $C_6$-$C_{12}$-aryl, preferably phenyl, OH, $C_1$-$C_{10}$-alkoxy, preferably $C_1$-$C_6$-alkoxy, C(=O)-$C_1$-$C_{10}$-alkyl, preferably C(=O)-$C_1$-$C_6$-alkyl, C(=O)-O-$C_1$-$C_{10}$-alkyl, preferably C(=O)-O-$C_1$-$C_6$-alkyl, CN, $NO_2$, F, Cl, Br, C(=O)N(R')$_2$, where R' are identical or different and are hydrogen or a $C_1$-$C_{10}$-alkyl radical, preferably $C_1$-$C_6$-alkyl radical, NH-C(=O)R', where R' has the meaning given above, or else, in each case two adjacent substituents $R^1$ together form a $C_2$-$C_{20}$-alkylene or $C_2$-$C_{20}$-alkylidene radical, preferably a $C_3$-$C_{10}$-alkylene or $C_3$-$C_{10}$-alkylidene radical, where these alkylene and alkylidene radicals may be interrupted once or more than once by O, COO or CO.

10. The process as claimed in claim 8, characterized in that olefins of the formula IIa are oxidized to oxiranes of the formula IIb



IIa



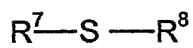
IIb

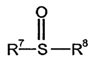
where

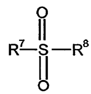
$R^2$, $R^3$, $R^4$ and $R^5$, independently of one another, are H, $C_1$-$C_{10}$-alkyl, preferably $C_1$-$C_6$-alkyl $C_3$-$C_{10}$-cycloalkyl, preferably $C_3$-$C_6$-cycloalkyl, $C_6$-$C_{12}$-aryl, preferably phenyl, OH, $C_1$-$C_{10}$-alkoxy, preferably $C_1$-$C_6$-alkoxy, C(=O)-$C_1$-$C_{10}$-alkyl, preferably C(=O)-$C_1$-$C_6$-alkyl, C(=O)-O-$C_1$-$C_{10}$-alkyl, preferably C(=O)-O-$C_1$-$C_6$-alkyl, CN, $NO_2$, F, Cl, Br, C(=O)N(R')$_2$, where R' are identical or different and are hydrogen or a $C_1$-$C_{10}$-alkyl radical, preferably $C_1$-$C_6$-alkyl radical, NH-C(=O)R', where R' has the

meaning given above, or else, in each case two adjacent radicals from the group of $R^{2\text{-}5}$ together form a $C_2$-$C_{20}$-alkylene or $C_2$-$C_{20}$-alkylidene radical, preferably a $C_3$-$C_{10}$-alkylene or $C_3$-$C_{10}$-alkylidene radical, where these alkylene and alkylidene radicals may be interrupted once or more than once by O, COO or CO.

11. The process as claimed in claim 8, characterized in that sulfides of the formula IIIa are oxidized to sulfoxides of the formula IIIb and to sulfones of the formula IIIc,


IIIa

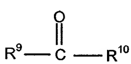

IIIb

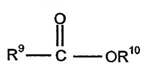

IIIc

where

$R^7$ and $R^8$ are identical or different and and are H, $C_1$-$C_{10}$-alkyl, preferably $C_1$-$C_6$-alkyl, $C_3$-$C_{10}$-cycloalkyl, preferably $C_3$-$C_6$-cycloalkyl, or $C_6$-$C_{12}$-aryl, preferably phenyl, or else the two substituents $R^7$ and $R^8$ together form a $C_2$-$C_{20}$-alkylene or $C_2$-$C_{20}$-alkylidene radical, preferably $C_4$-$C_{10}$-alkylene or $C_4$-$C_{10}$-alkylidene radical, where these alkylene and alkylidene radicals may be interrupted once or more than once by O, COO or CO.

12. The process as claimed in claim 8, characterized in that ketones of the formula IVa are oxidized to esters of the formula IVb,


IVa


IVb

where

$R^9$ and $R^{10}$ are identical or different and are H, $C_1$-$C_{10}$-alkyl, preferably $C_1$-$C_6$-alkyl, $C_3$-$C_{10}$-cycloalkyl, preferably $C_3$-$C_6$-cycloalkyl, or $C_6$-$C_{12}$-aryl, preferably phenyl, or else the two substituents $R^9$ and $R^{10}$ together form a $C_2$-$C_{20}$-alkylene or $C_2$-$C_{20}$-alkylidene radical, preferably $C_3$-$C_{10}$-alkylene or $C_3$-$C_{10}$-alkylidene radical, where these alkylene and alkylidene radicals may be interrupted once or more than once by O, COO or CO.

| COMBINED DECLARATION AND POWER OF ATTORNEY | ATTORNEY DOCKET NO |
| --- | --- |
| | |

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name. I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought
on the invention entitled

**METHOD FOR OXIDATING ORGANIC COMPOUNDS**

the specification of which is attached hereto,

or was filed on **June 23, 2000**

as a PCT Application Serial No. **PCT/EP00/05829**

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims.

I acknowledge the duty to disclose information which is material to the patentability of this application in accordance with Title 37, Code of Federal Regulations, §1.56.

I hereby claim foreign priority benefits under Title 35, United States Code, §119 of any foreign application(s) for patent or inventor's certificate listed below and have also identified below any foreign application for patent or inventor's certificate having a filing date before that of the application on which priority is claimed:

Prior Foreign Application(s), the priority(ies) of which is/are to be claimed:

| | | |
| --- | --- | --- |
| **199 30 960.4** | **Germany** | **July 5, 1999** |
| (Number) | (Country) | (Month/Day/Year Filed) |

I hereby claim the benefit under Title 35, United States Code, §120 of any United States application(s) listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States application in the manner provided by the first paragraph of Title 35, United States Code, §112, I acknowledge the duty to disclose the material information as defined in Title 37, Code of Federal Regulations, §1.56 which occured between the filing date of the prior application and the national or PCT international filing date of this application:

| | | |
| --- | --- | --- |
| (Application Serial No.) | (Filing Date) | (Status)<br>(patented, pending, abandoned) |
| (Application Serial No.) | (Filing Date) | (Status)<br>(patented, pending, abandoned) |

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

**POWER OF ATTORNEY: As a named inventor, I hereby appoint the following attorney(s) and this application and to transact all business in the Patent and Trademark Office conne**

**JOSEPH C. GIL, Patent Office Registration Number 26,602 ARON PREIS, Patent Office Registration Number 29,426 LYNDANNE M. WHALEN, Patent Office Registration Number 29,457 THOMAS W. ROY, Patent Office Registration Number 29,582 RICHARD E. L. HENDERSON, Patent Office Registration Number 31,619 GODFRIED R. AKORLI, Patent Office Registration Number 28,779 N. DENISE BROWN, Patent Office Registration Number 36,097 NOLAND J. CHEUNG, Patent Office Registration Number 39,138 DIDERICO VAN EYL, Patent Office Registration Number 38,641 CAROLYN M. SLOANE, Patent Office Registration Number 44,339 JAMES R. FRANKS, Patent Office Registration Number 42,552 JACKIE ANN ZURCHER, Patent Office Registration Number 42,251 RAYMOND J. HARMUTH, Patent Office Registration Number 33,896**

**all of Bayer Corporation, Pittsburgh, Pennsylvania 15205-9741**

**Send Correspondence To: Direct Telephone Calls To:**
**Patent Department**
**Bayer Corporation (412) 777-2349**
**100 Bayer Road**
**Pittsburgh, Pennsylvania 15205-9741**

| | | |
|---|---|---|
| FULL NAME OF SOLE OR FIRST INVENTOR<br>Reinhard Langer | INVENTOR'S SIGNATURE | DATE<br>2001-12-06 |
| RESIDENCE<br>D 47918 Tönisvorst, Germany DEY | | CITIZENSHIP<br>German |
| POST OFFICE ADDRESS<br>c/o Bayer Aktiengesellschaft, D 51368 Leverkusen, Germany | | |
| FULL NAME OF SECOND INVENTOR<br>Alexander Klausener | INVENTOR'S SIGNATURE | DATE<br>2001-12-10 |
| RESIDENCE<br>D 50259 Pulheim, Germany DEY | | CITIZENSHIP<br>German |
| POST OFFICE ADDRESS<br>c/o Bayer Aktiengesellschaft, D 51368 Leverkusen, Germany | | |
| FULL NAME OF THIRD INVENTOR<br>Lars Rodefeld | INVENTOR'S SIGNATURE | DATE<br>2001-12-07 |
| RESIDENCE<br>D 51375 Leverkusen, Germany DEX | | CITIZENSHIP<br>German |
| POST OFFICE ADDRESS<br>c/o Bayer Aktiengesellschaft, D 51368 Leverkusen, Germany | | |
| FULL NAME OF FOURTH INVENTOR | INVENTOR'S SIGNATURE | DATE |
| RESIDENCE | | CITIZENSHIP |
| POST OFFICE ADDRESS | | |
| FULL NAME OF FIFTH INVENTOR | INVENTOR'S SIGNATURE | DATE |
| RESIDENCE | | CITIZENSHIP |
| POST OFFICE ADDRESS | | |
| FULL NAME OF SIXTH INVENTOR | INVENTOR'S SIGNATURE | DATE |
| RESIDENCE | | CITIZENSHIP |
| POST OFFICE ADDRESS | | |
| FULL NAME OF SEVENTH INVENTOR | INVENTOR'S SIGNATURE | DATE |
| RESIDENCE | | CITIZENSHIP |
| POST OFFICE ADDRESS | | |